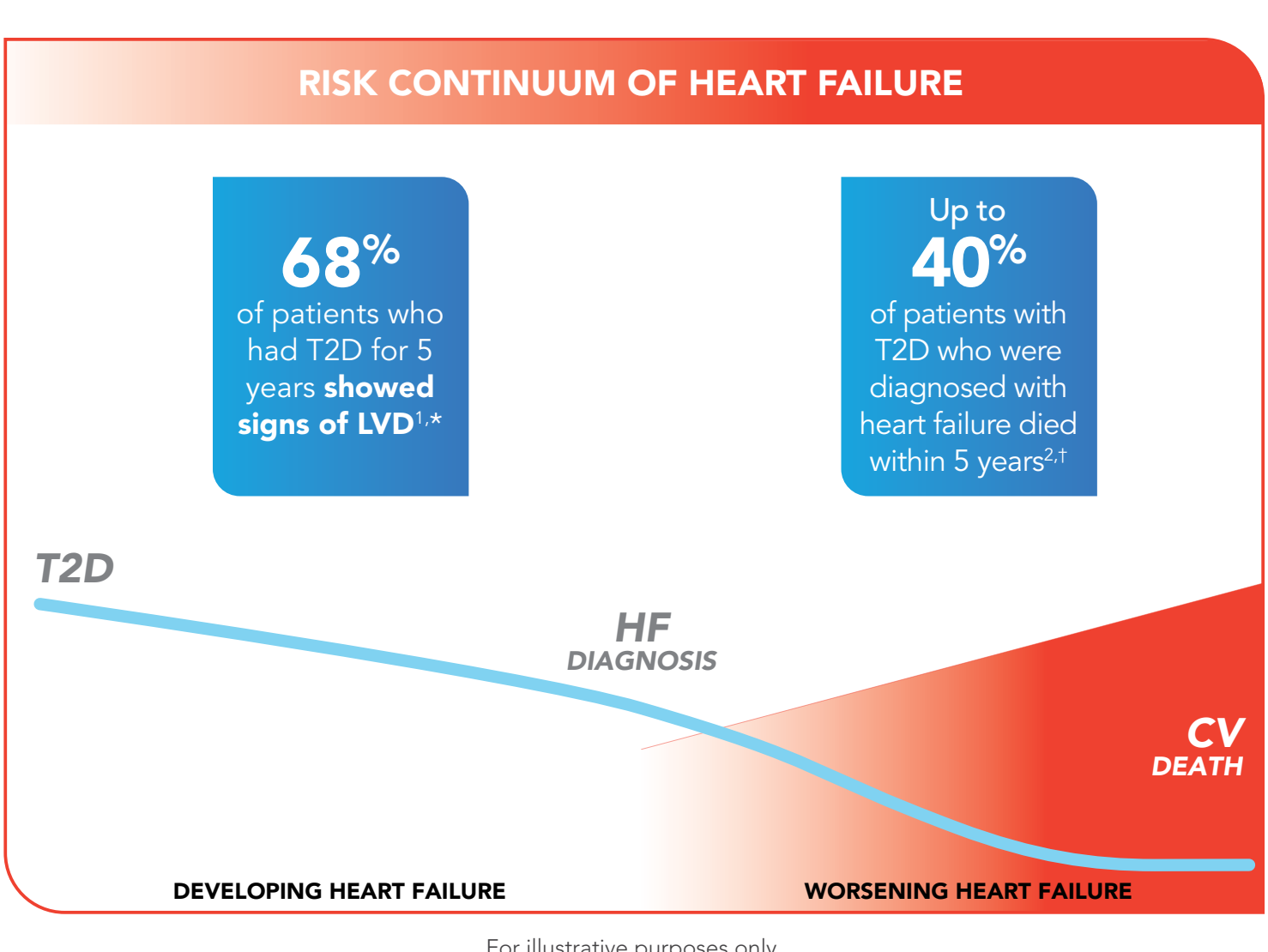
farxiga (dapagliflozin) 5mg & 10mg tablets

FOR ADULTS WITH T2D AND MULTIPLE CV RISK FACTORS

It's never too early, until it's too late



For illustrative purposes only.

- Controlling glucose alone has not been shown to reduce the risk of HF in patients with T2D[3,‡]

Act early for your patients who are at increased risk for hospitalization for heart failure

*Prospective, multicenter study evaluating clinical and echocardiographic characteristics of individuals with T2D (N=386) who were determined to be free from cardiac disease. Mean duration of diabetes was 5 years; mean A1C was 7.1%. LVD comprised of the combined asymptomatic left ventricular systolic and/or diastolic dysfunction.[1]

†Data based on a study of 46,720 Medicare patients with T2D who developed heart failure between 1994 and 1999.[2]

‡Heart failure resulting in hospitalization or death.[3]

Indications and Limitations of Use for FARXIGA

FARXIGA is indicated to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular (CV) disease or multiple CV risk factors.

FARXIGA is not recommended for patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

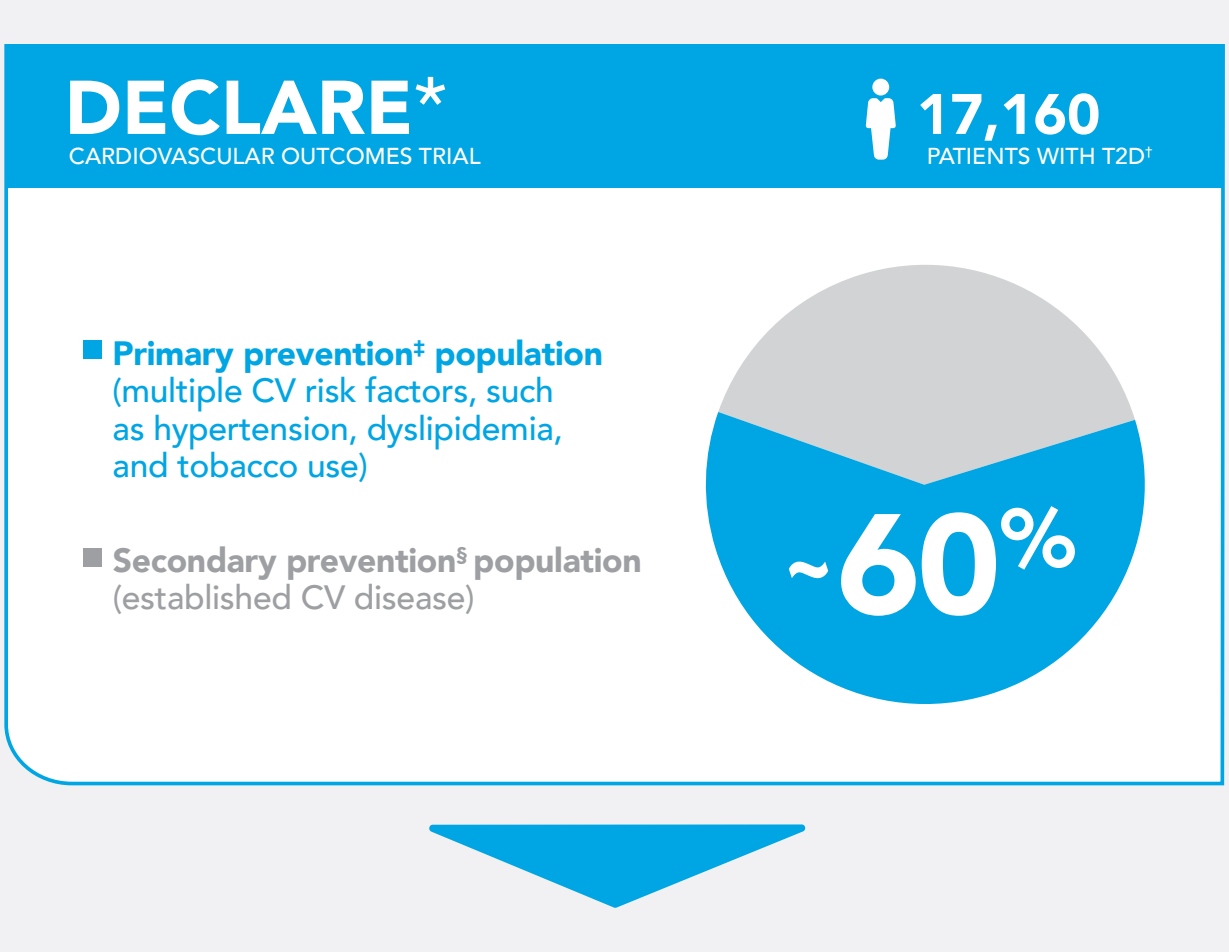
Important Safety Information for FARXIGA

Contraindications

- Prior serious hypersensitivity reaction to FARXIGA
- Patients with severe renal impairment (eGFR <30 mL/min/1.73 m²) being treated for glycemic control without established CV disease or multiple CV risk factors
- Patients on dialysis

A1C=glycated hemoglobin; CV=cardiovascular; eGFR=estimated glomerular filtration rate; HF=heart failure; LVD=left ventricular dysfunction; T2D=type 2 diabetes.

DECLARE: The largest CVOT with an SGLT2i to study hospitalization for heart failure risk reduction in both primary *and* secondary prevention patients[4-8]



FARXIGA is the only SGLT2i studied in a CVOT with a majority of primary prevention patients[4-6]

*DECLARE was a randomized, double-blind, placebo-controlled, multicenter trial designed to evaluate the effect of FARXIGA 10 mg compared with placebo on CV outcomes in adults with T2D and multiple CV risk factors or established CV disease.[4]

†Patients included were ≥40 years of age.[9]

‡Primary prevention defined as multiple CV risk factors (age ≥55 years in men or ≥60 years in women and at least 1 of the following: dyslipidemia, hypertension, or current tobacco use) and without a history of a CV event at baseline.[4]

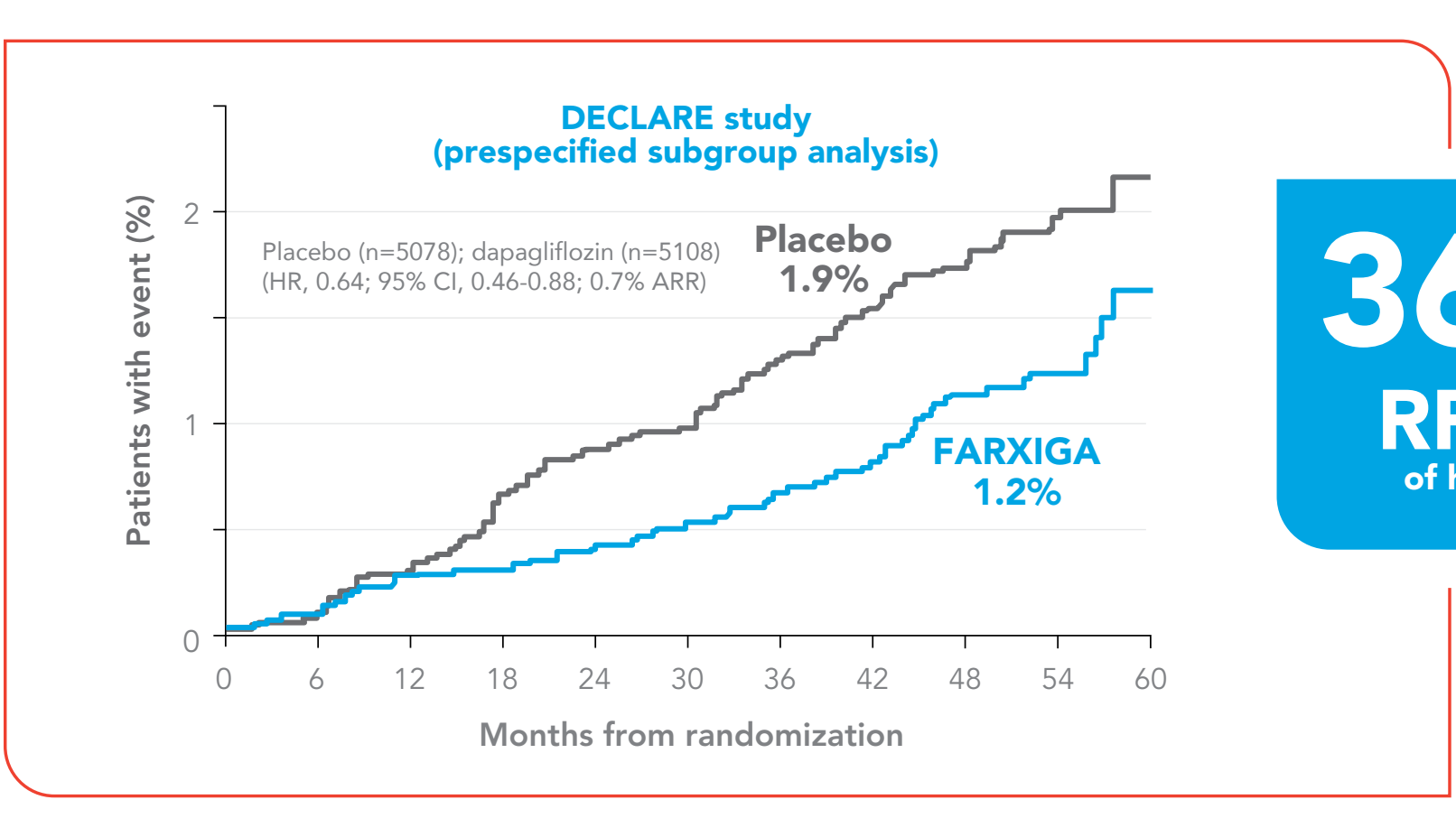
§Secondary prevention defined as established CV disease (clinically evident ischemic heart disease, ischemic cerebrovascular disease, or peripheral arterial disease).[9]

CV=cardiovascular; CVOT=cardiovascular outcomes trial; DECLARE=Dapagliflozin Effect on Cardiovascular Events; SGLT2i=sodium-glucose cotransporter 2 inhibitor; T2D=type 2 diabetes.

IN ADULTS WITH TYPE 2 DIABETES AND MULTIPLE CV RISK FACTORS

Add FARXIGA today to help keep your patients out of the hospital due to heart failure

In primary prevention patients* (multiple CV risk factors), FARXIGA is indicated to reduce the risk of hospitalization for heart failure[4,9,10,†]



36% RRR of hHF

27% RRR for hospitalization for heart failure‡ in the overall patient population (component of the primary end point); (HR, 0.73; 95% CI, 0.61-0.88; 0.8% ARR)[10]

- 22% RRR for hospitalization for heart failure in patients with established CV disease (secondary prevention§); (HR, 0.78; 95% CI, 0.63-0.97; 1.2% ARR)[11]
- FARXIGA met the primary safety end point vs placebo for the composite of CV death, MI, or ischemic stroke (MACE); (HR, 0.93; 95% CI, 0.84-1.03) *P*<0.001 (noninferiority).[9] FARXIGA is not indicated to reduce the risk of MACE

*Primary prevention defined as multiple CV risk factors (age ≥55 years in men or ≥60 years in women and at least 1 of the following: dyslipidemia, hypertension, or current tobacco use) and without a history of a CV event at baseline.[4]

†Data represented as event rates over a median follow-up of 4.2 years.

‡Hospitalization for heart failure indication is not limited by diabetic nephropathy or the presence of macroalbuminuria.

§Secondary prevention defined as established CV disease (clinically evident ischemic heart disease, ischemic cerebrovascular disease, or peripheral arterial disease).[11]

ARR=absolute risk reduction; CV=cardiovascular; DECLARE=Dapagliflozin Effect on Cardiovascular Events; hHF=hospitalization for heart failure; HR=hazard ratio; MACE=major adverse cardiovascular events; MI=myocardial infarction; RRR=relative risk reduction.

Well-established safety profile

Safety data from the DECLARE study in patients with type 2 diabetes[9]

Select AEs of interest, %	FARXIGA 10 mg (n=8574)	Placebo (n=8569)
Amputation	1.4%	1.3%
Acute kidney injury	1.5%	2.0%
Fracture	5.3%	5.1%
Major hypoglycemia	0.7%	1.0%
Symptoms of volume depletion	2.5%	2.4%
Urinary tract infection	1.5%	1.6%
Genital infection*	0.9%	0.1%
Diabetic ketoacidosis	0.3%	0.1%
Fournier's Gangrene	0.01%	0.06%

*Leading to discontinuation of the trial regimen or considered to be serious AEs.

Important Safety Information for FARXIGA (cont'd)

Warnings and Precautions

- **Volume Depletion:** FARXIGA can cause intravascular volume depletion which may manifest as symptomatic hypotension or acute transient changes in creatinine. Acute kidney injury requiring hospitalization and dialysis has been reported in patients with type 2 diabetes receiving SGLT2 inhibitors, including FARXIGA. Patients with impaired renal function (eGFR less than 60 mL/min/1.73 m²), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Before initiating FARXIGA in these patients, assess volume status and renal function. After initiating therapy, monitor for signs and symptoms of hypotension and renal function
- **Ketoacidosis in Diabetes Mellitus** has been reported in patients with type 1 and type 2 diabetes receiving FARXIGA. Some cases were fatal. Assess patients who present with signs and symptoms of metabolic acidosis for ketoacidosis, regardless of blood glucose level. If suspected, discontinue FARXIGA, evaluate and treat promptly. Before initiating FARXIGA, consider risk factors for ketoacidosis. Patients on FARXIGA may require monitoring and temporary discontinuation in situations known to predispose to ketoacidosis
- **Urosepsis and Pyelonephritis:** SGLT2 inhibitors increase the risk for urinary tract infections (UTIs) and serious UTIs have been reported with FARXIGA. Evaluate for signs and symptoms of UTIs and treat promptly
- **Hypoglycemia:** FARXIGA can increase the risk of hypoglycemia when coadministered with insulin and insulin secretagogues. Consider lowering the dose of these agents when coadministered with FARXIGA
- **Necrotizing Fasciitis of the Perineum (Fournier's Gangrene):** Rare but serious, life-threatening cases have been reported in patients with diabetes mellitus receiving SGLT2 inhibitors including FARXIGA. Cases have been reported in females and males. Serious outcomes have included hospitalization, surgeries, and death. Assess patients presenting with pain or tenderness, erythema, swelling in the genital or perineal area, along with fever or malaise. If suspected, institute prompt treatment and discontinue FARXIGA

Well-established safety profile across clinical trials

Pooled safety data for FARXIGA across clinical studies[4]

AEs in 12 placebo-controlled studies of glycemic control reported in ≥2% of patients treated with FARXIGA†	FARXIGA 5 mg (n=1145)	FARXIGA 10 mg (n=1193)	Placebo (n=1193)
Female genital mycotic infections‡	8.4%	6.9%	1.5%
Nasopharyngitis	6.6%	6.3%	6.2%
Urinary tract infections	5.7%	4.3%	3.7%
Back pain	3.1%	4.2%	3.2%
Increased urination	2.9%	3.8%	1.7%
Male genital mycotic infections‡	2.8%	2.7%	0.3%
Nausea	2.8%	2.5%	2.4%
Influenza	2.7%	2.3%	2.3%
Dyslipidemia	1.5%	2.5%	1.5%
Constipation	2.2%	1.9%	1.5%
Discomfort with urination	1.5%	2.1%	0.7%
Pain in extremity	2.0%	1.7%	1.4%

†AEs were evaluated with FARXIGA 5 mg and 10 mg in 12 placebo-controlled studies ranging from 12 to 24 weeks. FARXIGA was studied as monotherapy in 4 studies, and in 8 studies as add-on to background antidiabetic therapy or as combination with metformin.

‡n for females: FARXIGA 5 mg=581, FARXIGA 10 mg=598, placebo=677; n for males: FARXIGA 5 mg=564, FARXIGA 10 mg=595, placebo=716.

Important Safety Information for FARXIGA (cont'd)

Adverse Reactions

In a pool of 12 placebo-controlled studies, the most common adverse reactions (≥5%) associated with FARXIGA 5 mg, 10 mg, and placebo respectively were female genital mycotic infections (8.4% vs 6.9% vs 1.5%), nasopharyngitis (6.6% vs 6.3% vs 6.2%), and urinary tract infections (5.7% vs 4.3% vs 3.7%).

AE=adverse event; DECLARE=Dapagliflozin Effect on Cardiovascular Events; eGFR=estimated glomerular filtration rate; SGLT2=sodium-glucose cotransporter 2.

The treatment algorithm has changed

FARXIGA IS THE ONLY SGLT2i RECOMMENDED TO HELP PREVENT HOSPITALIZATION FOR HEART FAILURE

In the AACE 2020 update to the Comprehensive Type 2 Diabetes Management Algorithm[12]

NEW AACE GUIDANCE FOR TYPE 2 DIABETES INCLUDES

- Regardless of glycemic control, an SGLT2i with proven efficacy (ie, dapagliflozin) is recommended as first-line treatment to reduce hospitalization for heart failure for patients at high risk for ASCVD, or with established ASCVD or HFrEF
- Dapagliflozin **is the only SGLT2i recommended to help prevent hospitalization for heart failure** and demonstrate efficacy in HFrEF

The ADA 2020 guidelines recommend an SGLT2i with proven benefits (ie, dapagliflozin) to reduce the risk of hospitalization for heart failure[13]

AACE=American Association of Clinical Endocrinologists; ADA=American Diabetes Association; ASCVD=atherosclerotic cardiovascular disease; HFrEF=heart failure with reduced ejection fraction; SGLT2i=sodium-glucose cotransporter 2 inhibitor.

Convenient once-daily dosing

Once-daily dosing

To reduce the risk of hospitalization for heart failure in adults with T2D and established CV disease or multiple CV risk factors

10 MG

RECOMMENDED DOSE

FARXIGA tablet shown is not actual size.

AM dosing | **With or without food**

- In patients with volume depletion, correct this condition prior to initiation of FARXIGA
- FARXIGA can cause intravascular volume depletion which may manifest as symptomatic hypotension or acute transient changes in creatinine. Acute kidney injury requiring hospitalization and dialysis has been reported in patients with type 2 diabetes receiving SGLT2 inhibitors, including FARXIGA. Patients with impaired renal function (eGFR less than 60 mL/min/1.73 m²), elderly patients, or patients on loop diuretics may be at increased risk for volume depletion or hypotension. Before initiating FARXIGA in these patients, assess volume status and renal function. After initiating therapy, monitor for signs and symptoms of hypotension and renal function

Important Safety Information for FARXIGA (cont'd)

Use in Specific Populations

- **Pregnancy:** Advise females of potential risk to a fetus especially during the second and third trimesters
- **Lactation:** FARXIGA is not recommended when breastfeeding

CV=cardiovascular; eGFR=estimated glomerular filtration rate; SGLT2=sodium-glucose cotransporter 2; T2D=type 2 diabetes.

Access to affordable medications is necessary for patients* with type 2 diabetes at risk of hospitalization for heart failure

ACCESS: FARXIGA is covered without prior authorization for the majority of your patients†

AFFORDABILITY: $0 per month for most commercial patients‡

*"Patients" means covered lives (commercial, employer, federal programs, FEHBP, municipal plan, PBM, union) at tiers 1-3 preferred in the nation, as calculated by Fingertip Formulary® as of February 22, 2019.

†"Covered without prior authorization" means that additional information is not required to be provided to the health plan in order for FARXIGA to be covered. Step edits may apply.

‡As low as $0 for as long as you prescribe any available dose of FARXIGA.

It's never too early, until it's too late

In patients with type 2 diabetes and multiple cardiovascular risk factors, confront the risk of hospitalization for heart failure early with FARXIGA

farxiga (dapagliflozin) 5mg & 10mg tablets

Indications and Limitations of Use for FARXIGA® (dapagliflozin)

FARXIGA is indicated:

- to reduce the risk of hospitalization for heart failure in adults with type 2 diabetes mellitus and established cardiovascular (CV) disease or multiple CV risk factors
- as an adjunct to diet and exercise to improve glycemic control in adults with type 2 diabetes mellitus
- to reduce the risk of cardiovascular death and hospitalization for heart failure in adults with heart failure (NYHA class II-IV) with reduced ejection fraction

FARXIGA is not recommended for patients with type 1 diabetes mellitus or for the treatment of diabetic ketoacidosis.

Important Safety Information for FARXIGA

Contraindications

- Prior serious hypersensitivity reaction to FARXIGA
- Patients with severe renal impairment (eGFR <30 mL/min/1.73 m²) being treated for glycemic control without established CV disease or multiple CV risk factors
- Patients on dialysis

Warnings and Precautions

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- **Genital Mycotic Infections:** FARXIGA increases the risk of genital mycotic infections, particularly in patients with prior genital mycotic infections. Monitor and treat appropriately

Adverse Reactions

In a pool of 12 placebo-controlled studies, the most common adverse reactions (≥5%) associated with FARXIGA 5 mg, 10 mg, and placebo respectively were female genital mycotic infections (8.4% vs 6.9% vs 1.5%), nasopharyngitis (6.6% vs 6.3% vs 6.2%), and urinary tract infections (5.7% vs 4.3% vs 3.7%).

Use in Specific Populations

- **Pregnancy:** Advise females of potential risk to a fetus especially during the second and third trimesters
- **Lactation:** FARXIGA is not recommended when breastfeeding

DOSING

- To reduce the risk of hospitalization for heart failure in patients with T2D and established CV disease or multiple CV risk factors, the recommended dose of FARXIGA is 10 mg orally once daily
- To improve glycemic control in patients with T2D, the recommended starting dose of FARXIGA is 5 mg orally once daily, taken in the morning. In patients tolerating FARXIGA 5 mg once daily who require additional glycemic control, the dose can be increased to 10 mg once daily
- To reduce the risk of CV death and hospitalization for heart failure in patients with HFrEF, the recommended dose of FARXIGA is 10 mg orally once daily

Please read US Full Prescribing Information and Medication Guide for FARXIGA.

You may report side effects related to AstraZeneca products by clicking here.

References: 1. Faden G, Faganello G, De Feo S, et al. The increasing detection of asymptomatic left ventricular dysfunction in patients with type 2 diabetes mellitus without overt cardiac disease: data from the SHORTWAVE study. *Diabetes Res Clin Pract.* 2013;101(3):309-316. **2.** Bertoni AG, Hundley WG, Massing MW, Bonds DE, Burke GL, Goff DC Jr. Heart failure prevalence, incidence, and mortality in the elderly with diabetes. *Diabetes Care.* 2004;27(3):699-703. **3.** Turnbull FM, Abraira C, Anderson RJ, et al. Intensive glucose control and macrovascular outcomes in type 2 diabetes. *Diabetologia.* 2009;52(11):2288-2298. **4.** FARXIGA® (dapagliflozin) [package insert]. Wilmington, DE: AstraZeneca Pharmaceuticals LP; 2020. **5.** Invokana® (canagliflozin) [package insert]. Titusville, NJ: Janssen Pharmaceuticals, Inc; 2020. **6.** Jardiance® (empagliflozin) [package insert]. Ridgefield, CT: Boehringer Ingelheim Pharmaceuticals, Inc; 2020. **7.** Steglatro™ (ertugliflozin) [package insert]. Whitehouse Station, NJ: Merck & Co, Inc; 2020. **8.** Cannon CP, McGuire DK, Pratley R, et al. Design and baseline characteristics of the eValuation of ERTugliflozin efficacy and Safety CardioVascular outcomes trial (VERTIS-CV). *Am Heart J.* 2018;206:11-23. **9.** Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N Engl J Med.* 2019;380(4):347-357. **10.** Data on File, REF-62129; AstraZeneca Pharmaceuticals LP. **11.** Supplementary appendix to: Wiviott SD, Raz I, Bonaca MP, et al. Dapagliflozin and cardiovascular outcomes in type 2 diabetes. *N Engl J Med.* 2019;380(4):347-357. **12.** Garber AJ, Handelsman Y, Grunberger G, et al. Consensus statement by the American Association of Clinical Endocrinologists and American College of Endocrinology on the comprehensive type 2 diabetes management algorithm—2020 executive summary. *Endocr Pract.* 2020;26(1):107-139. **13.** American Diabetes Association. 10. Cardiovascular disease and risk management: Standards of Medical Care in Diabetes—2020. *Diabetes Care.* 2020;43(Suppl 1):S111-S134.

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